

**REMARKS**

Figure 1 and Figure 3, and claims 13, 16, and 17, have been amended to incorporate SEQ ID NOs.

Pursuant to the requirements of 37 C.F.R. §§ 1.821-1.825, Applicant submits the enclosed Sequence Listing and computer readable form (CRF). The amino acid sequences disclosed in the specification, claims, and drawings may be found in computer readable form in file 001525.txt on the enclosed diskette and are presented in the paper copy of the Sequence Listing, also enclosed.

Applicant hereby certifies that the information recorded in computer readable form (CFR) supplied on the enclosed diskette as file 001525.txt is identical to the written Sequence Listing. The material presented in computer readable form is not new matter because it presents sequences the same as those disclosed in the specification, as filed.

The required copy of the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures is also enclosed.

Applicant believes that the requirements of 37 C.F.R. §§ 1.821-1.825 have been met.

Respectfully submitted,

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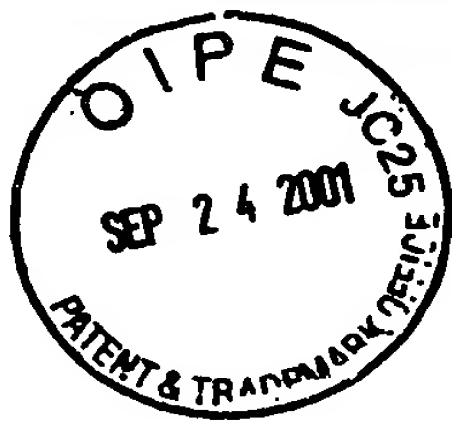
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Serial No. 09/728,670  
Atty. Docket No.: 702-001525

**MARKED-UP VERSION OF THE CLAIMS**

13. (Once Amended) A staphylokinase derivative having essentially the amino acid sequence as depicted in figure 3 **(SEQ ID NO: 10)** in which one or more encircled or boxed amino acids have been replaced by another amino acid thus reducing the absorption of SakSTAR-specific antibodies from plasma of patients treated with staphylokinase and further incorporating one or more polyethylene glycol groups.

16. (Once Amended) Staphylokinase derivatives SakSTAR(K35X, G36X, E65X, K74X, E80X, D82X, K102X, E108X, K109X, K121X, K130X, K135X, K136X, +137X) having the amino acid sequence as depicted in Figure 1 **(SEQ ID NO: 10)** in which the amino acids Lys in position 35, Gly in position 36, Glu in position 65, Lys in position 74, Glu in position 80, Asp in position 82, Lys in position 102, Glu in position 108, Lys in position 109, Lys in position 121, Lys in position 130, Lys in position 135 and/or Lys in position 136 have been replaced with other amino acids and/or in which one amino acid has been added at the COOH-terminus, thus altering the immunogenicity after administration in patients, and further incorporating at least one polyethylene glycol group.

17. (Once Amended) Staphylokinase derivatives listed in Tables 1, 2, 3, 4, 5, 6, 7 and 8, having the amino acid sequence depicted in figure 3 **(SEQ ID NO: 10)** in which the boxed or encircled amino acids have been replaced by other amino acids thus reducing the absorption of SakSTAR-specific antibodies from plasma of patients treated with staphylokinase, without reducing the specific activity, the derivative further incorporating at least one polyethylene glycol group.

New Staphylokinase Derivatives  
Desiré José Collen  
Atty. Docket No. 702-001525

1														14
Ser	Ser	Ser	Phe	Asp	Lys	Gly	Lys	Tyr	Lys	Lys	Gly	Asp	Asp	
15														28
Ala	Ser	Tyr	Phe	Glu	Pro	Thr	Gly	Pro	Tyr	Leu	Met	Val	Asn	
29														42
Val	Thr	Gly	Val	Asp	Ser	Lys	Gly	Asn	Glu	Leu	Leu	Ser	Pro	
43														56
His	Tyr	Val	Glu	Phe	Pro	Ile	Lys	Pro	Gly	Thr	Thr	Leu	Thr	
57														70
Lys	Glu	Lys	Ile	Glu	Tyr	Tyr	Val	Glu	Trp	Ala	Leu	Asp	Ala	
71														84
Thr	Ala	Tyr	Lys	Glu	Phe	Arg	Val	Val	Glu	Leu	Asp	Pro	Ser	
85														98
Ala	Lys	Ile	Glu	Val	Thr	Tyr	Tyr	Asp	Lys	Asn	Lys	Lys	Lys	
99														112
Glu	Glu	Thr	Lys	Ser	Phe	Pro	Ile	Thr	Glu	Lys	Gly	Phe	Val	
113														126
Val	Pro	Asp	Leu	Ser	Glu	His	Ile	Lys	Asn	Pro	Gly	Phe	Asn	
127														136
Leu	Ile	Thr	Lys	Val	Val	Ile	Glu	Lys	Lys					

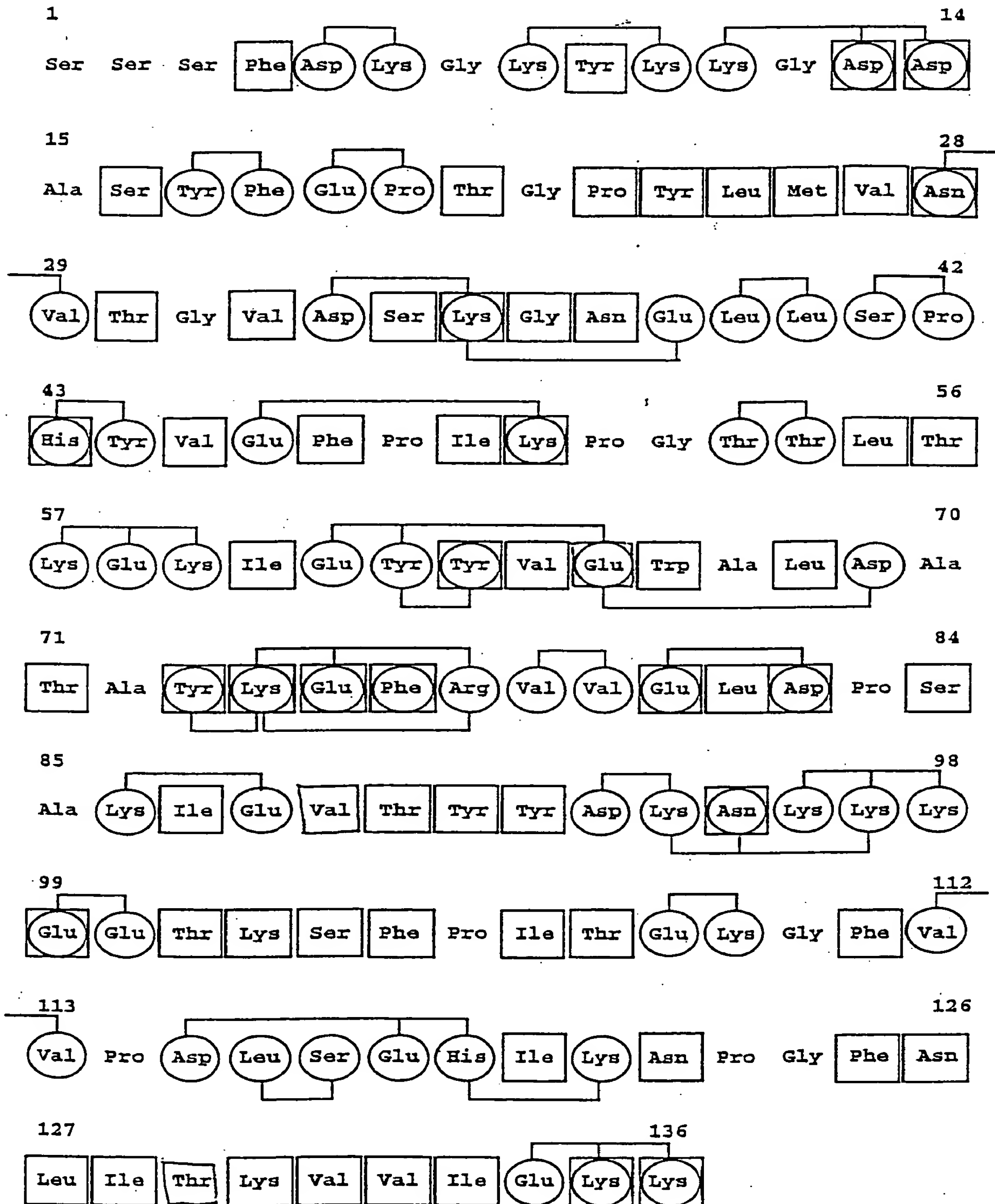
SEQ ID NO: 10

Figure 1

New Staphylokinase Derivatives

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Atty. Docket No. 702-001525



SEQ ID NO: 10



: single amino acid to Ala substitution



: combined (2 or 3) amino acid to Ala substitutions

Figure 3